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ROLE OF THE LOCUS COERULEUS IN DEVELOPMENT OF CEREBROVASCULAR DISTURBANCES IN ACUTE MYOCARDIAL ISCHEMIA

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The development of cardiac arrhythmias in acute myocardial ischemia has been shown to be preceded by changes in electrical activity of the locus coeruleus (LC), and preliminary coagulation of LC under these conditions considerably reduces the intensity of the arrhythmia [4]. Disturbances of the cerebral hemodynamics also have been found in acute myocardial ischemia [3] and stimulation of LC is accompanied by slowing of the cerebral blood flow [6, 8-10].

In the investigation described below changes in the cerebral blood flow were studied during acute myocardial ischemia after coagulation of LC.

EXPERIMENTAL METHOD

Experiments were carried out on 24 noninbred male rats weighing 200-240 g, anesthetized with sodium pentobarbital (25 mg/kg) and artificially ventilated (succinylcholine 0.2 mg/kg).

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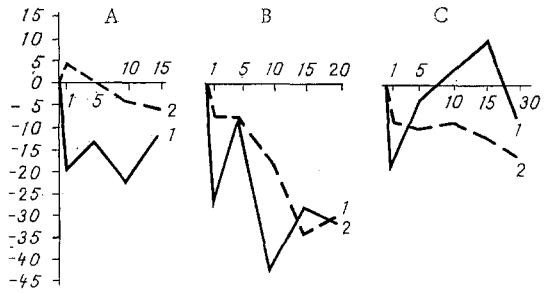

Fig. 1. Changes in total cerebral blood flow (1) and blood pressure (2) during electrical stimulation of LC (A), acute myocardial ischemia (B), and acute myocardial ischemia after coagulation of LC (C). Abscissa, time (in min); ordinate, changes in total cerebral blood flow and blood pressure (in % of initial).

TABLE 1. Changes (in % of initial values) in Total Cerebral Blood Flow (TCB) and Blood Pressure (BP) in Response to Electrical Stimulation of LC (A), Occlusion of Coronary Artery (B), and Occlusion of Coronary Artery after Coagulation of LC (C) (M ± m)

Time, min	A		B		C	
	TCB	BP	TCB	BP	TCB	BP
0	118±8,9	92±9,0	108±14,5	92±4,2	154±37,1	88±8,5
1	—20,4±6,1*	3,8±4,8	—27,7±13,2	—8,7±8,6	—20,1±10,1	—9,0±2,2*
5	—14,4±5,8	0	—9,2±8,4	—9,2±8,5	—4,4±15,9	—10,2±2,5*
10	—23,787,2*	—3,2±3,4	—42,5±5,9*	—18,4±3,8*	3,2±9.7**	—9,2±2,2**
15	—11,8±4,6*	—5,4±3,9	—27,5±9,3*	—33,6±4,6*	10,1±4,8	—12,5±1,9**
30			—31,7±6,2*	—30,4±5,7*	—7,2±2,4*	—18,1±6,4**

Legend. *P < 0.01 compared with initial value; **P < 0.05 compared with B.

The general cerebral blood flow and response of the blood pressure to electrical stimulation of LP were studied in all animals under the following conditions: intact heart (eight experiments), acute myocardial ischemia (eight experiments), acute myocardial ischemia + coagulation of LC (eight experiments).

The total cerebral blood flow (in ml/100 g/min) was determined by the hydrogen clearance method [5] in the unopened confluence of the sinuses, because hydrogen readily diffuses through the walls of the main arteries and veins [1]. A platinum plate electrode was applied with its active surface on the dura covering the confluence of the sinuses and secured to the cranial bones with melted wax. The animal was given three or four artificial inhalations of pure hydrogen and the clearance curve was recorded.

Electrodes for electrical stimulation and electrical coagulation of LC were inserted in accordance with coordinates from the stereotaxic atlas [7]: A = 7.4, L = 1.0, H = 6.0. Bipolar nichrome electrodes, coated with enamel except at the tips for 0.5 mm, and each 50 μm in diameter (interelectrode distance 100 μm) were used for electrical stimulation. LC was stimulated by pulses with a frequency of 100 Hz, duration 1 msec, and amplitude 10-15 V for 10 sec. The total cerebral blood flow began to be measured after restoration of the blood pressure (1-2 min after stimulation), which was recorded in the carotid artery. Electrical coagulation of LC was produced by passing a steady current of 5 mA for 10-15 sec through nichrome electrodes (diameter 100 μm), coated with enamel except at the tip (0.5 mm). Acute myocardial ischemia was produced by high ligation of the left anterior coronary artery 30-40 min after coagulation of LC. Cardiac activity was monitored by recording the ECG in three standard leads. After each experiment the accuracy of insertion of the stimulating electrodes and the region of coagulation were verified in sections cut on a freezing microtome.

EXPERIMENTAL RESULTS

Electrical stimulation of LC in animals with an intact heart slowed the outflow of blood from the brain. The most marked effect was observed at the 1st (20.4 ± 6.1%, P < 0.05) and 10th (23.7 ± 7.2%, P < 0.05) minutes after stimulation, and it lasted more than 15 min (Fig. 1). During this time interval no statistically significant changes were observed in blood pressure (Table 1).

After high ligation of the coronary artery the total cerebral blood flow did not change statistically significantly during the first 5 min (Table 1). Later a considerable fall was observed in the blood flow, and by the 10th minute it was only 42.5 ± 5.9% (P < 0.001). Maximal slowing of the cerebral blood flow in most experiments coincided in time with the appearance of cardiac arrhythmias of different types.

Changes in the cerebral blood flow after occlusion of the coronary artery and coagulation of LC differed significantly from those in animals with occlusion of the coronary artery alone. After coagulation of LC the total cerebral blood flow was lowered after cardiac ischemia by only 7.2 ± 2.4% ($P < 0.05$) by the 30th minute, whereas in the experiments without coagulation of LC it fell by 31.7 ± 6.2% ($P < 0.01$) by this time (Fig. 1C). At all other times changes observed in the blood flow were not significant (Table 1). The fall of blood pressure in animals of this group was statistically significant. However, the maximal hypotensive shift, observed in these animals by the 30th minute, was reduced almost by half compared with that in animals with acute myocardial ischemia but without coagulation of LC.

The experiments thus showed that hyperactivation of LC by electrical stimulation caused a decrease in the cerebral blood flow. Coagulation of LC prevented the cerebrovascular disturbances arising during acute myocardial ischemia. The most profound disorders of the cerebral hemodynamics associated with occlusion of the coronary artery preceded the appearance of cardiac arrhythmias in animals in which LC was not coagulated beforehand. Activated adrenergic neurons of LC in acute myocardial ischemia probably acquired the role of a hyperactive determinant structure [2], whose activity led, on the one hand, to an even more marked disturbance of cardiac function and, on the other hand, to a disturbance of the cerebral hemodynamics. This latter effect may play the role of secondary pathogenetic factor, contributing to the further disturbance of regulation of the ischemic heart.

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